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Beautiful summary by AMENSupport friend and Mayo Clinic Rochester GI oncologist Dr. Thor Halfdanarson on how he follows well-differentiated metastatic NETs

Well differentiated NETs span the Ki67 proliferation spectrum of 0% to well above 50% and have a very variable, and at times unpredictable, history.

Grade 3 well differentiated NETs are increasingly recognized. A general rule, but not perfect, is that higher Ki67 predicts more aggressive tumors. Tumor grade (assigned by Ki67) and differentiation of the tumor (requires an experienced pathologist), are both crucial elements of evaluation. In recent months, I have seen 2 well differentiated cases with Ki67 index > 90%. Patients with G3 NETs will often need a different strategy for monitoring than patients with G1 NETs. Similarly, a G2 NET with Ki67 of 4% is expected to be more indolent than a G2 NET with Ki67 of 19%. Therefore, a “one size fits all” strategy will never be appropriate for monitoring patients with advanced well differentiated NETs.

The primary location also seems to matter, but according to some studies, pancreatic NETs are more aggressive than small bowel NETs.

A reasonable strategy is cross-sectional imaging every 3-6 months, and CT is the most convenient method. There is

usually no reason to routinely image the chest, as thoracic metastases are uncommon.

For patients with liver-predominant metastases, an MRI may provide better results, often with gadoxetic acid (Eovist) as contrast. If a CT is used, careful attention to contrast timing is crucial and both arterial and venous phase imaging is needed as NET liver mets can be very hard to see. All too often, CT imaging is inappropriately done.

The interval between scans depends on several factors, most importantly the clinical course of the disease, which usually is apparent after a few scans. In indolent NETs, even if metastatic, imaging every 12 months may be appropriate for some. The treatment status also matters, but not all patients with metastatic NETs need therapy.

Ga68 (maybe soon Cu64...) DOTATATE PET CT (NETSPOT) is discouraged for follow-up, as the association with SUV changes is incompletely associated with clinical course, and tumor size is near impossible to measure with precision. Ga68 DOTA PET may be useful to monitor patients with bone-predominant metastases, but has little role in monitoring patients with visceral mets (the majority of patients).

Tumor markers have little or no role for monitoring. Although markers such as chromogranin A (CgA) may correlate with prognosis, CgA is a challenging marker with multiple concerns (unreliable in patients on PPIs) there are no studies to support their use in clinical decision making; but one such trial is actively accruing patients and will hopefully add to our knowledge of CgA as a marker for making decisions.

There is still a lot of room for refining monitoring strategies for well differentiated NETs (G1-G3), but the forthcoming NANETS guidelines on managing advanced pancreatic NETs will provide some guidance.
So in summary:

- Cross sectional imaging (CT or MRI) every 3-6 months is appropriate and one will soon "feel out" the behavior of the disease and adjust imaging intervals accordingly
- One size does NOT fit all
- There is no role for routine Ga68 DOTATATE PET imaging (although bone dominant disease may be an exception where it helps)
- Routine use of markers is not helpful for clinical decision making (but data may be on the way)